240. (New) The method of Claim 238 wherein the mammal is a human.

#### **REMARKS**

#### Examiner Interview

Applicants' representatives thank the Examiner for conducting a telephonic interview on September 16, 2002. During the interview, amendment of the claims to more particularly define the invention was discussed. In addition, given the number of claims and amendments, the Examiner and Applicants agreed that re-numbering of the claims in consecutive order would assist in examination of the pending claims. Accordingly, Applicants cancelled the claims and presented them once again in consecutive order. All claims have support in the application and claims as originally filed, as described in more detail below.

#### Claim Amendments

Claims 3-6, 10, 11, 42, 72, 74, 76-79, 82, 84-152 have been cancelled and new Claims 153-240 have been added. New Claims 153-155, 157-162, 174-176, 178-183, 195, 196, 198-207, 209-213, 215-224, 226-233 and 235-237 read on the elected species.

Independent Claim 153 is based on cancelled claim 3. Claim 153 recites "artery-specific Ephrin family ligand" and "vein-specific Eph family receptor." Support for this recitation is found, for example, in the specification at page 3, line 7 *et seq.* and in Claim 3 as originally filed.

Dependent Claims 154, 155 and 156 are based on cancelled Claims 4, 76 and 6, respectively.

Independent Claim 157 is based on cancelled Claims 5 and 76.

Dependent Claims 158, 159, 160 and 161 are based on cancelled Claims 118, 119, 120 and 129, respectively.

Independent Claim 163 is based on cancelled Claims 4 and 6.

Dependent Claim 164 is based on cancelled Claims 4.

Dependent Claim 165 is based on cancelled Claims 101 and 104.

Support for dependent Claims 166 and 187 is found, for example, in the specification at page 17, lines1-6, page 29, lines 8-15 and page 30, lines 3-14.

Dependent Claim 166 is based on cancelled Claims 101 and 104.

Dependent Claim 167 is based on cancelled Claims 102 and 104.

Dependent Claim 168 is based on cancelled Claims 109 and 113.

Dependent Claim 169 is based on cancelled Claims 110 and 114.

Dependent Claim 170 is based on cancelled Claims 111 and 115.

Dependent Claims 171 and 172 are based on cancelled Claims 126 and 127, respectively.

Independent Claim 174 is based on cancelled Claim 94.

Dependent Claims 175, 176 and 177 are based on cancelled Claims 96, 116 and 107, respectively.

Independent Claim 178 is based on cancelled Claims 100 and 116.

Dependent Claims 179, 180, 181 and 182, are based on cancelled Claims 125, 118, 120 and 129, respectively.

Independent Claim 184 is based on cancelled Claims 95 and 107.

Dependent Claim 185 is based on cancelled Claims 96.

Dependent Claim 186 is based on cancelled Claims 101 and 104.

Dependent Claim 188 is based on cancelled Claims 102 and 104.

Dependent Claim 189 is based on cancelled Claims 109 and 113.

Dependent Claim 190 is based on cancelled Claims 110 and 114.

Dependent Claim 191 is based on cancelled Claims 111 and 115.

Dependent Claims 192 and 193 are based on cancelled Claims 126 and 127, respectively.

Independent Claim 195 is based on cancelled Claim 10. Claim 10 recites "artery-specific Ephrin family ligand." Support for this recitation is found, for example, in the specification at page 3, line 7 *et seq.* and in Claim 10 as originally filed.

Dependent Claims 196, 197, 198, 199, 200, 201, 202, 203 and 204 are based on cancelled Claims 72, 78, 134, 82, 138, 139, 140, 141 and 142, respectively.

Dependent Claims 205 and 206 are based on cancelled Claim 11.

Dependent Claims 207, 208, 209, 210 and 211 are based on cancelled Claims 79, 11, 149, 150 and 151, respectively.

Independent Claim 213 is based on cancelled Claim 133.

Dependent Claims 214, 215, 216, 217, 218, 219, 220, 221, 222, 223 and 224 are based on cancelled Claims 135, 136, 134, 137, 138, 139, 140, 141, 142, 143 and 146, respectively.

Dependent Claim 225 is based on cancelled Claims 11 and 147.

Dependent Claim 226 is based on cancelled Claims 79 and 148.

Dependent Claims 227, 228, 229 and 230 are based on cancelled Claims 149, 150, 151 and 152, respectively.

Independent Claim 232 is based on cancelled Claim 42. Claim 42 recites "artery-specific Ephrin family ligand" and "vein-specific Eph family receptor." Support for this recitation is found, for example, in the specification at page 3, line 7 *et seq.* and in Claim 42 as originally filed.

Dependent Claims 233 and 234 are based on cancelled Claims 85 and 84, respectively.

Independent Claim 235 is based on cancelled Claims 74 and 85.

Dependent Claim 236 is based on cancelled Claim 87.

Independent Claim 238 is based on cancelled Claims 74 and 84.

Dependent Claim 239 is based on cancelled Claim 87.

Support for new Claims 162, 173, 183, 194, 212, 231, 237 and 240 is found, for example, in the specification at page 10, lines 13-15.

The new Claims are supported by the subject application as originally filed. Therefore, this Amendment adds no new matter. Claims readable on the elected species are Claims 153-155, 157-162, 174-176, 178-183, 195, 196, 198-207, 209-213, 215-224, 226-233 and 235-237.

Additional remarks addressing the Examiner's rejections are set forth below.

# Paragraph 3. Rejection of Claims 3, 5, 42, 76, 77, 85, 89-91, 93, 94, 98-102, 116, 121-126 and 129-132 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected Claims 3, 5, 42, 76, 77, 85, 89-91, 93, 94, 98-102, 116, 121-126 and 129-132 under 35 U.S.C. § 112, first paragraph, as lacking enablement commensurate with the scope of the claims.

As stated by the Examiner, "the original basis of this rejection was that, while one of skill in the art could identify ephrin/eph pairs in arteries and veins, one of skill in the art could not predict that they would be involved in angiogenesis." Office Action, page 2, lines 19-21. Further, as stated by the Examiner, "Applicant's arguments are sufficient to overcome the original basis of the rejection, that one of skill could not predictably find other eph receptors and ephrin ligands that are involved in angiogenesis." Office Action, page 3, lines 9-11.

In the Examiner's opinion, however, one of skill in the art would still not be able to use the invention as broadly claimed, because what is required for Applicants' invention is that enhancing the interaction between an eph receptor and an ephrin ligand result in angiogenesis and that addition of a soluble eph receptor result in angiogenesis. Office Action, page 3, line 15 to page 4, line 2. The Examiner states that "Applicant has provided no guidance to indicate that a soluble receptor would enhance, rather than inhibit, angiogenesis" and "[t]here are no teachings in the specification that would allow one of skill in the art to predict the outcome of using such a receptor." Office Action, page 4, lines 3-8.

Applicants have presented new claims which do not require enhancement of the interaction between the Ephrin family ligand and the Eph family receptor (see, e.g., new independent Claim 157 which is drawn to a method of enhancing angiogenesis comprising administering an agonist of an artery-specific Ephrin family ligand or an agonist of a vein-specific Eph family receptor and new independent Claim 178 which is drawn to a method of enhancing angiogenesis comprising administering an agonist of EphrinB2 or an agonist of EphB4). Support for an agonist of an artery-specific Ephrin family ligand or a vein-specific Eph family receptor enhancing angiogenesis is provided in the specification (e.g., Specification, page 30, lines 3-30). Applicants' specification further discloses soluble agonists (e.g., Specification, page 30, lines 15-30) and cites other teachings of soluble agonists (see, e.g., Specification, page 30, lines 18-25, citing Wang et al., Neuron 18:383-396 (Reference AY, of record) and Stein et al., Genes Dev. 12:667-678 (1998) (Reference AT, of record)).

Thus, in view of the teachings in Applicants' specification and the knowledge available in the art at the time of Applicants' invention (e.g., as evidenced by the teachings of Wang *et al.*, (Reference AY, of record) and Stein *et al.*, (Reference AT, of record)), it is Applicants' belief

that new Claims 153-194, which do not require enhancement of the interaction between an Ephrin family ligand and Eph family receptor, are enabled and allowable.

### Paragraph 4. Rejection of Claims 10, 72, 79 and 82 Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected Claims 10, 72, 79 and 82 under 35 U.S.C. § 112, second paragraph, because the claims do not require that the ligand be expressed on arterial cells. New Claim 195 (which is based on cancelled independent Claim 10) recites "a component which binds an artery-specific Ephrin family ligand." It is therefore Applicants' belief that this rejection is obviated and that new Claims 195-231 are in condition for allowance.

# Paragraph 5. Objection to Claims 3, 10, 42, 74, 76, 77, 85, 94, 116, 125, 126, 129, 130-134, 136-138, 143-149, 151 and 152

The Examiner has objected to Claims 3, 10, 42, 74, 76, 77, 85, 94, 116, 125, 126, 129, 130-134, 136-138, 143-149, 151 and 152, because they encompass non-elected inventions or depend from claims that encompass non-elected inventions. In view of Applicants' presentation of new Claims 153-240 and for the reasons outlined above, it is Applicants' belief that all Claims are in condition for allowance.

As indicated above, New Claims 153-155, 157-162, 174-176, 178-183, 195, 196, 198-207, 209-213, 215-224, 226-233 and 235-237 read on the elected species. As stated in the Office Action dated March 8, 2000, the Examiner is respectfully reminded that:

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Examiner's Office Action dated March 8, 2000, page 3, lines 14-18.

#### Request for Interview

Applicants' Attorney respectfully requests that the Examiner contact her prior to issuing the next Office Communication.

## **CONCLUSION**

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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